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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,182	01/18/2002	Pier Giuseppe Pelicci	Mewburn	6367

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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
01/08/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/937,182	PELICCI ET AL.	
	Examiner	Art Unit	
	J. Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38 and 42-52* is/are pending in the application.

4a) Of the above claim(s) *1-8,11,13-18,26,28-35,38 and 42-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9,10,12,19-25,27,36,37 and 46-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 September 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/11/02 12/21/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

This Action is in response to the communication filed on 10/9/2007.

The amendment filed 10/9/2007 is acknowledged and has been entered.

Claims 1-38, 42-52 are currently pending in the application and are addressed herein.

Election/Restrictions

Applicant's election with traverse of Group II (claims 9, 10, 12, 19, 20-25, 27, 36, 37, 46-52) and the species "vascular complications of diabetes" in the reply filed on 10/9/2007 is acknowledged. The traversal is on the ground(s) that (1) a lack of unity was not set forth in the international stage of examination, (2) the inventive concept is that p66Shc acts in a pathway that regulates stress response and this was not recognized in the art including the cited anticipatory reference (Migliaccio et al.) thus it can not be reasonably maintained that the reference can be anticipatory, (3) The separation of claims into Groups II and V and wholly improper as claim 9 is generic to both groups and searching Groups II and V would not impose a serious burden on the examiner and at the very least Groups II and V should be rejoined. This is not found persuasive because: (1) the fact that a lack of unity was not set forth in the international stage does not preclude a lack of unity finding in the national stage, (2) Migliaccio et al. is an anticipatory reference because, as previously indicated, Migliaccio et al. teach transfecting a cell with the plasmid that expresses p66shc, thus modulating (i.e., increasing) expression of a p66shc polypeptide in the transfected cell. It is noted the increasing expression ofp66shc in a cell, such as by the method taught by Migliaccio et al., would necessarily modulate resistance to oxidative stress in the cell. Migliaccio et al. also teach p66shc mutants embraced by claim 1. Therefore,

Migliaccio et al. is anticipatory to at least claims 1, 9 and 14. Since claims 1, 9 and 14 are anticipated by Migliaccio et al., there can be no special technical feature linking these claims, (3) search burden is not a consideration in determining unity of invention. It is noted that applicants are correct that claim 9 is generic to Groups II and V. Therefore claim 9 is a linking claim that links Inventions II and V. Therefore claim 9 is subject to linking claim practice.

Specifically, claim 9 link(s) the inventions of Groups II and V. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claim 9. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Therefore, the separation of Groups II and V is proper as long as the linking claim (claim 9) is not allowable. Since claim 9 is not allowable (for the reasons indicated herein), the restriction between Groups II and V is still deemed proper. Therefore, Applicants arguments are not persuasive.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-8 11, 13-18, 26, 28-35, 38, 42-45 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/9/2007.

Information Disclosure Statement

1. The information disclosure statement (IDS) submitted on 12/11/2002 and 12/21/2007 are acknowledged. The submissions are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

Specification Objection – Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Specifically, Figure 5 contains sequences which require sequence identifiers (SEQ ID NOS), but no sequence identifier is present. Furthermore, the sequences must be included in the Sequence Listing. It is noted that the sequence identifier can be presented in either the Figure itself or in the Brief Description in the specification. In this case, no sequence identifiers can be found for the sequences of Figure 5 either in the Figure or in the Brief Description. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the objection

can be withdrawn. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Claim Rejections - 35 USC § 112, second paragraph

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 9, 12, 19-25, 27, 36, 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Method claims require an active or positive step that accomplishes the goals for the method which were stated in the method's preamble. The instant claims lack such a step and are confusing because the additional method step(s) is not sufficiently set forth. While minute details are not required in method claims, at least the basic steps must be recited in a positive, active fashion. See Ex parte Erlich, 3 USPQ2d1011, p.1011 (Bd. Pat. App. Int. 1986). For example, in claim 9 the steps presented are simply a method of contacting a cell with an agent that modulated p66shc expression. There is no requirement or active or positive step in the claims that said contacting modulates resistance to oxidative stress in the cell. This is indefinite because it leaves the scope of the claim unclear as to whether it is required that the resistance to oxidative stress is actually modulated in the cell.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claim 9 is rejected under 35 U.S.C. 102(b) as being anticipated by Migliaccio et al. (EMBO Journal, previously of record).

Migliaccio et al. teach transfecting a cell with a plasmid which expresses p66shc (e.g., see page 709, column 2; page 710, column 1; page 714, column 2; page 715, column 1). It is noted the increasing expression ofp66shc in a cell, such as by the method taught by Migliaccio et al., would necessarily modulate resistance to oxidative stress in the cell.

Applicant is reminded that MPEP 2112.01 teaches "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). 'When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.'"

Also see *Integra Life Sciences I Ltd. v. Merck KGaA,* 50 USPQ2d 1846 (DC SCalif, 1999) which teaches that a reference teaching a process may anticipate claims drawn to a method comprising the same process steps, despite the recitation of a different intended use in the preamble or the later discovery of a particular property of one of the starting materials or end products; and, *Ex parte Novitski*, 26 USPQ2d 1389 (Bd. Pat. App. & Inter. 1993), which teaches

that a reference teaching a claimed process, wherein one of the claimed properties of a product used in the prior art process is inherent but undisclosed by the reference, may be properly applied as art against the claimed process.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 9, 10, 12, 19-25, 27, 36, 37 and 46-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

First, the claims encompass a genus of p66shc molecules which are not adequately described by the instant disclosure. It is noted that the claims do not set forth any particular

sequence for p66shc molecules encompassed by the claims. Furthermore, it is respectfully pointed out that the specification specifically indicates:

> The nucleic acid of the present invention may comprises a p66shc coding sequence which differs further from the wild type sequence or the sequence as shown in Fig. 5 in that it is a nucleic acid sequence that is an allele, mutant, variant or derivative, by way of nucleotide addition, insertion, substitution or deletion of the wild type sequence as illustrated in Fig. 5.

Therefore, the claims clearly encompass p66shc sequences which differ from the disclosed sequences. However, the specification does not clearly identify the critical structural elements which p66shc function. That is, since the structural elements which are critical for the function of p66shc have not been described, the required structure-function relationship has not been descried. As such, one of skill in the art would not be able to readily identify which molecules of the claimed genus of p66shc molecules would have the desired function and which one would not, without performing additional experimentation. Therefore, the specification has not adequately described the genus of p66shc molecules encompassed by the claims. The only member of the genus which appears to be adequately described is the amino acid sequence that is SEQ ID NO: 2 and the nucleotide sequences which would encode SEQ ID NO: 2 (which includes the sequence that is SEQ ID NO:1).

Additionally, the claims encompass a genus of agents that are capable of modulating p66shc expression. However, the specification does not adequately describe the genus of agents encompassed by the claims. It is noted that the broadest claims do not set forth any basic structural elements for the genus of p66shc expression modulators. Therefore, given the broadest reasonable interpretation, the claims can encompass a genus of agents that are not

structurally related. For instance, in the broadest embodiments, the agent could be a peptide, nucleic acid, small molecule, or another type of structurally distinct molecule. Accordingly, there can be no structural element common to all members of this diverse genus of molecules; and thus, no structure-function relationship can be established for the members of the claimed genus. Without a clear structure-function relationship, one of skill in the art would not be able to readily identify which molecules of the claimed genus of p66shc expression modulators, without performing additional experimentation. Furthermore, the claims could encompass p66shc expression modulators that have not yet been identified or created. Therefore, the specification has not adequately described the genus of p66shc expression modulator molecules encompassed by the claims. It is noted that the specification has described three specific member of the claims genus: (1) a polynucleotide sequence which encodes the p66shc sequence that is SEQ ID NO: 2 can be an inducer of p66shc expression, (2) an antisense nucleic acid sequence which specifically hybridizes to a nucleotide sequence which encodes the p66shc protein that is SEQ ID NO: 2 is an inhibitor of p66shc expression, and (3) a targeting vector which specifically targets and integrates into and disrupts expression of a sequence which encodes the p66shc protein that is SEQ ID NO: 2.

Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus of p66shc molecules and the genus of p66shc expression inhibitors encompassed by the claims.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in

possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of molecules, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).)

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Monday-Thursday 8:00 a.m.-6:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. E. Angell/
Primary Examiner
Art Unit 1635

Notice to Comply	Application No.	Applicant(s)	
	Examiner J. Eric Angell	Art Unit 1635	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other: _

Applicant Must Provide:

☒ An initial or **substitute** computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or **substitute** paper copy of the "Sequence Listing", as well as an amendment directing its entry into the **specification**.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216 or (703) 308-2923
For CRF Submission Help, call (703) 308-4212
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